	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments
1	BRS	L1	9932	second adj harmonic	USPAT; US-PGPUB; EPO; DERWENT	2002/10/01 11:01	
2	BRS	L2	266749	label or moiet$	USPAT; US-PGPUB; EPO; DERWENT	2002/10/01 11:01	
3	BRS	L3	543698	interface	USPAT; US-PGPUB; EPO; DERWENT	2002/10/01 11:01	
4	BRS	L4	53	1 same 2	USPAT; US-PGPUB; EPO; DERWENT	2002/10/01 11:01	
5	BRS	L5	13	3 and 4	USPAT; US-PGPUB; EPO; DERWENT	2002/10/01 11:08	
6	BRS	L6	42	4 and surface	USPAT; US-PGPUB; EPO; DERWENT	2002/10/01 11:08	

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments
7	BRS	L7	278	sum adj frequency adj generation	USPAT; US-PGPUB; EPO; DERWENT	2002/10/01 11:09	
8	BRS	L8	3	2 same 7	USPAT; US-PGPUB; EPO; DERWENT	2002/10/01 11:09	

ILE 'CAPLUS, MEDLINE, BIOSIS, CA, SCISEARCH, EMBASE' ENTERED AT 13:45:26
ON 01 OCT 2002

L1	38011	S SECOND (W) HARMONIC
L2	1372822	S LABEL# OR MARKER# OR TAG#
L3	60	S L1 (S) L2
L4	29	DUPLICATE REM L3 (31 DUPLICATES REMOVED)
L5	3470	S SUM (W) FREQUENCY (W) GENERATION
L6	3	S L2 (S) L5
L7	2	DUPLICATE REM L6 (1 DUPLICATE REMOVED)
L8	441	S SECOND (W) HARMONIC (W) IMAGING
L9	6	S L2 (S) L8
L10	2	DUPLICATE REM L9 (4 DUPLICATES REMOVED)
L11	1389	S DIFFERENCE (W) FREQUENCY (W) GENERATION
L12	3	S L2 (S) L11
L13	2	DUPLICATE REM L12 (1 DUPLICATE REMOVED)

4 ANSWER 3 OF 29 MEDLINE DUPLICATE 3

TI Three-dimensional high-resolution second-harmonic generation imaging of endogenous structural proteins in biological tissues.

AB We find that several key endogenous protein structures give rise to intense **second-harmonic** generation (SHG)-nonabsorptive frequency doubling of an excitation laser line. **Second-harmonic** imaging microscopy (SHIM) on a laser-scanning system proves, therefore, to be a powerful and unique tool for high-resolution, high-contrast, three-dimensional studies of live cell and tissue architecture. Unlike fluorescence, SHG suffers no inherent photobleaching or toxicity and does not require exogenous **labels**. Unlike polarization microscopy, SHIM provides intrinsic confocality and deep sectioning in complex tissues. In this study, we demonstrate the clarity of SHIM optical sectioning within unfixed, unstained thick specimens. SHIM and two-photon excited fluorescence (TPEF) were combined in a dual-mode nonlinear microscopy to elucidate the molecular sources of SHG in live cells and tissues. SHG arose not only from coiled-coil complexes within connective tissues and muscle thick filaments, but also from microtubule arrays within interphase and mitotic cells. Both polarization dependence and a local symmetry cancellation effect of SHG allowed the signal from species generating the **second harmonic** to be decoded, by ratiometric correlation with TPEF, to yield information on local structure below optical resolution. The physical origin of SHG within these tissues is addressed and is attributed to the laser interaction with dipolar protein structures that is enhanced by the intrinsic chirality of the protein helices.

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